PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cognitive control and daily affect regulation in major depression and borderline personality disorder: protocol for an experimental ambulatory assessment study in Berlin, Germany
AUTHORS	Schulze, Lars; Burkner, Paul Christian; Bohlander, Julian; Zetsche, Ulrike

VERSION 1 – REVIEW

REVIEWER	Sandra Schlicker Institute of Psychology Department of clinical psychology and psychotherapy Friedrich-Alexander University Erlangen-Nürnberg
REVIEW RETURNED	03-May-2018

GENERAL COMMENTS	The present study aims to examine the link between individual differences in cognitive control and disturbances in affect Dynamics and Regulation in daily life of MDD and BPD individuals. The study protocol is well written and of high relevance. However, there are some minor Points which should be addressed in a revision (number and lines correspond to the original page number of the manuscript in the top right hand Corner): 1. Page 4, line 44: "Affective disturbances in depression are characterized by both the experience of sustained negative affect i.e., affective inertia, 5, as well as difficulty experiencing positive affect." Please improve orthography. 2. Page 12, line 16: "Due to high rates of Axis-I and Axis-II comorbidity in BPD presence of comorbid disorders will be allowed for study inclusion with the exception of a current major depressive episode, substance dependency within the last 12 months, bipolar or psychotic disorders. " You stated that Axis-I and Axis-II comorbidity will not be an exclusion criteria. Please state, whether you plan on controlling for comorbidity in the analyses. 3. Page 14, line 2: " Given that individuals with BPD may have problems in correct emotion identification, the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used to assess the impact of ER strategies on negative affect." Please clarify how problems with a possible incorrect identification of emotions will be accounted for. 4. Page 18, line 16: "At the end of the second laboratory session, participants will be asked to put on an ECG chest belt to measure their resting state heart rate variability for a 5-minute period." Please clarify why you are assessing heart rate variability.

	5. Page 20, line 40: "The predictor variables of interest will be Group (BPD, MDD, CTL) and the specific Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing)." Please include all analyzed ER strategies and their in the introduction of the manuscript.

REVIEWER	Anne Guhn Charité - Universitätsmedizin Berlin Department of Psychiatry and Psychotherapy Charitéplatz 1 10117 Berlin
REVIEW RETURNED	14-May-2018

GENERAL COMMENTS	This study protocol by Schulze et al. describes an interesting approach to disentangle shared and disorder-specific deficits in emotion regulation between patients suffering from BPD versus depression. The manuscript is clearly written and easy to follow, except for the following minor concerns: 0. General remarks - the abbreviations AR and ER are intermixed throughout the entire manuscript 1. Introduction - p.4: Please include a reference for affective disturbances regarding positive emotions in depression 2. Methods and Analyses - p.14 (assessment of cognitive control): Does the assessment include a neuropsychological test battery? Patients with depression, but also those suffering from BPD, are more likely to show decreased neuropsychological task performance (e.g. digit span, verbal IQ, inhibitory control, phasic alertness, etc.) compared to HC. All tasks intended to evaluate cognitive control between groups should thus be corrected for baseline cognitive performance. - p.18: The intentions of the assessment of ECG and movement are unclear. If hypotheses for group differences exist, the introductory section will benefit from a short theoretical part regarding the connection between ER with heart rate variability and with physical activity. - p.20 (data-analysis): How do the authors handle use of multiple ER strategies (reappraisal, rumination, …)? How is the intensity of the ER strategy assessed? Is that the "impact of ER strategy" that is stated on page 14? If so, this should be more clearly stated, e.g. by using the same terminology.

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VERSION 1 – AUTHOR RESPONSE

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Reviewer: 1 Reviewer Name: Sandra Schlicker Comment #1. Page 4, line 44: "Affective disturbances in depression are characterized by both the experience of sustained negative affect i.e., affective inertia, 5, as well as difficulty experiencing positive affect." Please improve orthography. Response: We apologizes for this messy sentence. We have corrected this sentence, which now reads follows (also see page 4): "Affective disturbances in depression are characterized by both the experience of sustained negative affect (i.e., affective inertia, 5) as well as difficulty experiencing positive affect 6 ." Comment #2. Page 12, line 16: "Due to high rates of Axis-I and Axis-II comorbidity in BPD presence of comorbid disorders will be allowed for study inclusion with the exception of a current major depressive episode, substance dependency within the last 12 months, bipolar or psychotic disorders.

" You stated that Axis-I and Axis-II comorbidity will not be an exclusion criteria. Please state, whether you plan on controlling for comorbidity in the analyses. Response: Descriptive details on the kind and number of comorbid diagnoses in the two clinical samples will be provided in each publication. In addition, all analyses will be repeated including the Brief Symptom List (BSI) total score as a covariate to check whether total symptom severity (across all main and comorbid disorders) has an impact on affect regulation or cognitive control. We prefer including the BSI total score as a covariate over including all sort of different comorbid diagnoses to keep the level of model complexity at an appropriate level. This important information is now given on page 13: "To control for the influence of total symptom severity, all analyses on group differences in affect regulation or cognitive control will be repeated including the Brief Symptom Inventory (BSI) total score as a covariate." Comment #3. Page 14, line 2: " Given that individuals with BPD may have problems in correct emotion identification, the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used to assess the impact of ER strategies on negative affect." Please clarify how problems with a possible incorrect identification of emotions will be accounted for. Response: Individuals with BPD have been found to show problems in the identification of specific emotions (i.e., anxiety). This means that although individuals with BPD are able to indicate how "bad" or "negative" they feel, they have problems specifying what exact emotion they experience (i.e., whether "bad" means anxious, or angry, or both, etc.). Thus, we won't use any specific emotion item as outcome measure because such items may not be a valid measure in individuals with BPD. Rather, we will use the mean value across all negative (or positive, respectively) emotion items. Thus, if a person with BPD feels angry at intensity 4 (on a scale from 1 to 7) but cannot tell whether this negative feeling is anger or anxiety or sadness, he or she might rate all negative emotion items with a 4. In this case, the sadness rating of 4 might not be correct (because the actual emotion is anger), but the mean negative affect rating of 4 is still valid. To make this clearer to the reader, we have slightly modified the above cited sentence. The sentence on page 15 now reads: "Given that individuals with BPD may have problems in correctly identifying specific negative emotions, only the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used to assess the impact of AR strategies on negative affect." Comment #4. Page 18, line 16: "At the end of the second laboratory session, participants will be asked to put on an ECG chest belt to measure their resting state heart rate variability for a 5- minute period." Please clarify why you are assessing heart rate variability. Response: The current research project focuses on affect regulation and cognitive control in borderline personality disorder, major depression, and healthy controls. However, the framework of this study allows to investigate some exciting additional research questions, such as the relation between heart rate variability and affect regulation, or the role of physical activity in daily affect dynamics. These additional research questions are now introduced at pages 10-11 in the revised manuscript: "6. Additional research questions The present research project allows to investigate several additional research questions that will be presented below: Heart rate variability and affect regulation: Thayer and Lane [48] proposed that heart rate variability reflects a psychophysiological index of affect regulation capacity. Indeed several studies illustrated that individuals with low resting vagally-mediated heart rate variability (vmHRV) have difficulties with affect regulation [49] [50]. Accordingly, lower HRV has been reported for individuals with BPD and MDD [51] [52], but to date no study directly assessed the role of vmHRV on affective dynamcis or affect regulation. In this study, we include a resting-state assessment of HRV to examine this question. Physical activity: There is considerable evidence that people feel better after being physically active [53]. However, these findings are almost entirely based on interventional, between-person designs. Hence, it is unclear whether these findings translate into daily life. It will thus be interesting to examine the associations between daily physical activity and daily affective states [54] . For these reasons, participants of our study are asked to wear an accelerometer during the ambulatory assessment phase. Expectation and recall biases of affective states: Depressive symptoms are associated with pronounced biases in the expectation and recall of affective states [55]. Notably, such biases also affect the choice and implementation of emotion regulation strategies [56] [57]. These processes, however, have been primarily investigated in non-clinical samples. In this study, depressed individuals and individuals with

BPD are asked to predict their average affect, sleep, and affect regulation before the ambulatory assessment phase. After the ambulatory assessment phase, they have to recall their average weekly affect, sleep, and affect regulation." Comment #5. Page 20, line 40: "The predictor variables of interest will be Group (BPD, MDD, CTL) and the specific Strategy (reappraisal, rumination, suppression, distraction, acceptance, social sharing)." Please include all analyzed ER strategies and their in the introduction of the manuscript. Response: The current research project focuses on three affect regulation strategies, namely rumination, suppression, and reappraisal. These AR strategies were chosen because they have attracted most attention in past research on depression and borderline personality disorder. Other AR strategies have been far less researched, and thus, the formulation of clear hypotheses regarding group differences in these strategies is not possible. The reason why we also ask about the implementation of other widely used AR strategies is to control for the overall degree of AR strategy use. This is important because individuals with a mental disorder generally use more AR strategies than healthy controls. Thus, when looking at the absolute numbers, it seems as if individuals with a mental disorder implement adaptive AR strategies more often than healthy indivi strategies than healthy controls. It is thus important to assess other relevant AR strategies to control for general strategy use. This information is now provided on page 5: "Please note that all hypotheses of the present project focus on these three most-researched AR strategies (i.e., rumination, suppression, reappraisal). When examining group differences in the use of specific AR strategies, however, it is important to control for overall AR strategy use 15. For this purpose, we also assess other widely used strategies, namely distraction, acceptance, and social sharing. Whereas findings on the association between distraction and depression are inconclusive 2 , there are hardly any studies on the association of acceptance or social sharing and depression. Thus, we do not formulate any specific hypotheses regarding these AR strategies. Reviewer: 2 Reviewer Name: Anne Guhn Comment #1.) The abbreviations AR and ER are intermixed throughout the entire manuscript Response: We thank the reviewer for pointing out this inconsistency. We now consistently speak of affect regulation (abbreviated as AR). Comment # 2.) Please include a reference for affective disturbances regarding positive emotions in depression Response: In accordance with this reviewers' comment, we have now included a reference to a meta-analysis showing that individuals with depression are characterized by considerably reduced emotional reactivity to positive stimuli (Bylsma, L. M., Morris, B. H., & Rottenberg, J. (2008). A meta-analysis of emotional reactivity in major depressive disorder. Clinical psychology review, 28(4), 676-691.). Comment # 3.) Does the assessment include a neuropsychological test battery? Patients with depression, but also those suffering from BPD, are more likely to show decreased neuropsychological task performance (e.g. digit span, verbal IQ, inhibitory control, phasic alertness, etc.) compared to HC. All tasks intended to evaluate cognitive control between groups should thus be corrected for baseline cognitive performance. Response: We agree with this reviewer that clinical samples show generally slowed processing speed leading to worse performance in a wide range of cognitive tasks. It is thus important to control for group differences in general processing speed. Please note, that all indices used to assess cognitive control in this research project are computed as the difference in response latencies between the experimental and the control condition in the respective experimental paradigm. Thus, these differences scores reflect specific deficits in cognitive control clear of any effect of general processing speed. In addition, group differences in intelligence will be controlled for by the subtest 4 of the Leistungsprüfsystem (LPS-4). This information is now provided on page 19: "Participants' intelligence will be estimated by assessing the subtest 4 of the Leistungsprüfsystem (LPS-4, Horn, 1983). This serves to control for group differences in basic cognitive capabilities when examining group differences in cognitive control." Comment #4.) The intentions of the assessment of ECG and movement are unclear. If hypotheses for group differences exist, the introductory section will benefit from a short theoretical part regarding the connection between ER with heart rate variability and with physical activity. Response: The current research project focuses on group differences in affect regulation and cognitive control. However, the framework of this study allows to investigate some exciting additional research questions, such as the relation between heart rate variability and affect regulation, or the role of physical activity in daily affect dynamics. These additional research questions

are now introduced at pages 10-11 in the revised manuscript: "6. Additional research questions The present research project allows to investigate several additional research questions that will be presented below: Heart rate variability and affect regulation: Thayer and Lane 48 proposed that heart rate variability reflects a psychophysiological index of affect regulation capacity. Indeed several studies illustrated that individuals with low resting vagally-mediated heart rate variability (vmHRV) have difficulties with affect regulation 49 50. Accordingly, lower HRV has been reported for individuals with BPD and MDD 51 52, but to date no study directly assessed the role of vmHRV on affective dynamcis or affect regulation. In this study, we include a resting-state assessment of HRV to examine this question. Physical activity: There is considerable evidence that people feel better after being physically active 53. However, these findings are almost entirely based on interventional, between-person designs. Hence, it is unclear whether these findings translate into daily life. It will thus be interesting to examine the associations between daily physical activity and daily affective states 54 . For these reasons, participants of our study are asked to wear an accelerometer during the ambulatory assessment phase. Expectation and recall biases of affective states: Depressive symptoms are associated with pronounced biases in the expectation and recall of affective states 55. Notably, such biases also affect the choice and implementation of emotion regulation strategies 56 57. These processes, however, have been primarily investigated in non-clinical samples. In this study, depressed individuals and individuals with BPD are asked to predict their average affect, sleep, and affect regulation before the ambulatory assessment phase. After the ambulatory assessment phase, they have to recall their average weekly affect, sleep, and affect regulation." Comment #5.) How do the authors handle use of multiple ER strategies (reappraisal, rumination, …)? How is the intensity of the ER strategy assessed? Is that the "impact of ER strategy" that is stated on page 14? If so, this should be more clearly stated, e.g. by using the same terminology. Response: We apologize for the lack of clarity in this respect. We assess the intensity of AR strategies by asking participants how much they used a respective strategy since the last beep. Answers are given on a 7-point Likert scale ranging from 1 (not at all) to 7 (very much). This information is given on page 15 in the revised manuscript: "Next, participants will be asked to indicate on a scale from 1 (not at all) to 7 (very much) how much they used the following strategies since the last beep: rumination ('I thought over and over again about a situation or my feelings'; 'How negative were these thoughts?'), suppression ('I controlled my emotion by not showing them'), reappraisal (I have thought about the situation in a different way.')." The "impact of a specific AR strategy" relates to the effectiveness of this AR strategy. This is examined by associating the use of a specific AR strategy to subsequent changes in affect ratings. In other words, the degree of using rumination between t-1 and t will be correlated with the change in affect between t-1 and t. Specifically, we will use hierarchical linear modeling with the respective affect rating (positive or negative) at time t as dependent variable, and affect ratings and strategy use at time t-1 as predictors. Multiple AR strategies will be entered as multiple predictors into the same multi-level model. We understand the confusion of this reviewer, because we mentioned the "impact of AR strategy analyses" at a point in the manuscript where this is not yet thoroughly explained to the reader. We have thus dropped this information in the above referenced sentence. The sentence on page 15 now reads: "Given that individuals with BPD may have problems in correctly identifying specific negative emotions, only the average score across all negative affect ratings (i.e., angry, anxious, ashamed, depressed, tense) will be used." When examining group differences in the frequency of using different AR strategies, we will compute three separate multi-level models with the intensity rating of the respective AR strategy (rumination, suppression, or reappraisal) at time t as dependent variable. The predictor variable of interest will be Group (BPD, MDD, CTL). In addition, we will enter the intensity rating of all other strategies to control for overall AR strategy use. This has now been clarified on page 21: "To examine whether groups differ in the frequency of using rumination, suppression, or reappraisal, we will employ hierarchical linear modeling. The dependent variable will be the intensity rating of the respective AR strategy assessed at time t. The predictor variable of interest will be Group (BPD, MDD, CTL). In addition, we will enter the intensity rating of all other strategies to control for overall AR strategy use."

REVIEWER	Sandra Schlicker Institute of Psychology Department of clinical psychology and psychotherapy Friedrich-Alexander University Erlangen-Nürnberg
REVIEW RETURNED	None declared.

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.

REVIEWER	Anne Guhn Charité - Universitätsmedizin Berlin Department of Psychiatry and Psychotherapy Charitéplatz 1 10117 Berlin Germany
REVIEW RETURNED	25-Jun-2018

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.